

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference TL/CHB10476/503	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR00/02336	International filing date (<i>day/month/year</i>) 18 August 2000 (18.08.00)	Priority date (<i>day/month/year</i>) 19 August 1999 (19.08.99)
International Patent Classification (IPC) or national classification and IPC C07K 1/00		
Applicant INSTITUT PASTEUR DE LILLE		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>3</u> sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input checked="" type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 16 March 2001 (16.03.01)	Date of completion of this report 23 November 2001 (23.11.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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International application No.

PCT/FR00/02336

I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

- ☒ the international application as originally filed.
- ☐ the description, pages 1-6.8-22, as originally filed.
pages _____, filed with the demand,
pages 7, filed with the letter of 25 October 2001 (25.10.2001),
pages _____, filed with the letter of _____.
- ☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. 1-10, filed with the demand,
Nos. 11-14,16,17, filed with the letter of 25 October 2001 (25.10.2001),
Nos. 15, filed with the letter of 08 November 2001 (08.11.2001).
- ☐ the drawings, sheets/fig 1/6-6/6, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.

1. The present application does not meet the requirements of PCT Rule 13 for the following reasons:

Although Claim 17 of the present application includes a reference to Claim 5, it does not enable dependence between said two claims to be established. For this reason, Claim 17 remains independent and the objection of lack of unity of the application is maintained as follows:

There is no common link between Claims 1-16 (concerning peptide-hydrazides, the methods for preparing same and the therapeutic uses of same) and Claim 17 (concerning the use of N,N'-tri(Boc)hydrazinoacetic acid or N,N'-di(Boc)hydrazinoacetic acid in the preparation of peptide-hydrazines). These two inventions are distinct insofar as they appear to solve different types of problems, namely a pharmacological problem and a chemical synthesis problem.

Thus, the following inventions are considered not to have a common general concept:

Claims 1-16 concern peptide-hydrazide derivatives, the preparation of same and the use of same in the preparation of vaccines or of a diagnostic reagent. Claim 17 concerns the use of a reagent for preparing peptide-hydrazines, which are intermediates in the synthesis of peptide-hydrazides.

Moreover, the applicant's attention is drawn to the fact that a true dependence between Claim 17 and Claim 5 would render Claim 17 equivalent and

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient).

Continuation of: IV.

therefore redundant to Claim 6 of the present application.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-17	YES
	Claims		NO
Inventive step (IS)	Claims	1-17	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-17	YES
	Claims		NO

2. Citations and explanations

1. Reference is made to the following documents:

- D1: JOURNAL OF PEPTIDE RESEARCH, vol. 52, no. 9, 1998, pages 180-184: cited in the application
- D2: TETRAHEDRON LETTERS, vol. 37, no. 40, 1996, pages 7259-7263: cited in the application
- D3: JOURNAL OF PEPTIDE RESEARCH, vol. 54, no. 9, October 1999 (1999-10), pages 270-278
- D4: TETRAHEDRON LETTERS, vol. 41, 2000 (2000-01), pages 45-48
- D5: PROC. EUR. PEPT. SYMP., 25TH MEETING DATE 30-8 TO 6-9-1998. EDITORS: S. BAJUSZ & F. HUDECZ, 1999, pages 108-109

Although D4 is not part of the prior art according to the PCT, insofar as said document was accessible to the public on a date between the duly claimed priority date (06.12.1999) and the filing date of the application (18.08.2000), the IPEA gives notice that it will no longer be part of the prior art according to EPC Article 54(2) when it enters the regional phase.

2. Novelty (PCT Article 33(2)):

D2 (page 7259, compound 5) describes a peptide

carrying an acetylated hydrazide group on the epsilon amine of a lysine in the N-terminal position of the peptide.

D1 and D5 describe hydrazone peptides whereas D3 describes hydrazine peptides. For this reason, the novelty of **Claims 1-16** of the application is not affected by said documents.

Moreover, the applicant is informed that the subject matter of **Claim 17** may be considered to be novel in view of the documents cited, as was indicated in the first communication.

3. **Inventive step (PCT Article 33(3)):**

D2, which is the closest prior art, concerns the preparation of peptide-hydrazones so that modified peptides can be transported through the cytoplasmic membrane of intact cells. The products of the present application differ from D2 by the nature of the group modifying the peptide, which is a hydrazide group.

The problem to be solved by the present application consists in preparing modified peptides in such a way as to facilitate their transport into the cell. As the applicant has argued, the specific teaching of D2 relates to a method of hydrazone ligation in solution, between a peptide and an aldehyde. As the formation of hydrazide derivatives, such as the compound 5 of D2, is not the aim of said document, but an intermediate step in the formation of hydrazone bonds, a person skilled in the art would not be expected to use the teaching of D2 to form hydrazide peptide derivatives with the aim of transporting a peptide into a cell. It is recognized that in so doing, a person skilled in the art would be taking an inventive step.

For this reason, **Claims 1-16** of the present application satisfy the requirements of **PCT Article 33(3)**.

Since the subject matter of **Claim 18** has not been disclosed or suggested in the cited documents, said claim meets the requirements of **PCT Article 33(3)**.